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(75) Inventors/Applicants (*for US only*): FIGDOR, Carl, Gustav [NL/NL]; Westwal 54, NL-5211 DD Den Bosch (NL). TORENSMA, Ruurd [NL/NL]; Neushoornstraat 6, NL-6531 RP Nijmegen (NL).

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ANTIGEN UPTAKE RECEPTOR FOR CANDIDA ALBICANS ON DENDRITIC CELLS

(57) Abstract: Dendritic cells (DC) that express the type II C-type lectin DC-SIGN (CD209) are located in the submucosa of tissues, where they mediate HIV-1 entry. Interestingly, the pathogen *Candida albicans*, the major cause of hospital-acquired fungal infections, is found at similar sites. Here it is demonstrated that DC-SIGN is able to bind *Candida albicans* both in DC-SIGN transfected cell lines and in human monocyte derived DC. Moreover, in immature DC, DC-SIGN is able to internalize *Candida* in specific DC-SIGN enriched vesicles, distinct from those containing the mannose receptor (MR; CD206), which is another *Candida* receptor on DC. Together, these results demonstrate that *C. albicans* has two major receptors on human monocyte derived DC, these receptors being DC-SIGN and MR. Targeting of DC-SIGN offers novel opportunities to combat chronic forms of candidiasis.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/702 A61K38/08 A61K38/17 A61K39/395 A61P31/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, BIOSIS, EMBASE, WPI Data, PASCAL, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	CAMBI ALESSANDRA ET AL: "The C-type lectin DC-SIGN (CD209) is an antigen-uptake receptor for Candida albicans on dendritic cells." EUROPEAN JOURNAL OF IMMUNOLOGY. GERMANY FEB 2003, vol. 33, no. 2, February 2003 (2003-02), pages 532-538, XP001179716 ISSN: 0014-2980 the whole document --- -/-	1-32

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

25 February 2004

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 38338 A (CHEVALIER REYNALD ;MALLET JEAN MAURICE (FR); TRINEL PIERRE ANDRE () 31 May 2001 (2001-05-31) page 2, line 6 -page 3, line 9 page 4, line 27 -page 5, line 7 example 6.1 page 71 -page 86; example 8	1-6,8,9, 11-13, 15-17, 20,21, 24, 27-29, 31,32
X	WO 00 63251 A (UNIV NIJMEGEN ;TORENSMA RUURD (NL); FIGDOR CARL GUSTAV (NL); GEIJT) 26 October 2000 (2000-10-26) page 7, line 12 - line 21 page 7, line 29 -page 8, line 3 page 8, line 25 -page 9, line 15 page 10, line 19 -page 11, line 2 figures 7,8 examples 1-8 claims 1-26	1,2, 8-16, 20-25, 31,32
X	EP 1 046 651 A (KONINKL UNIVERSITEIT NIJMEGEN) 25 October 2000 (2000-10-25) the whole document	1,2, 8-16, 20-25, 31,32
X	WO 02 50119 A (STICHTING KATHOLIEKE UNIV ;TORENSMA RUURD (NL); FIGDOR CARL GUSTAV) 27 June 2002 (2002-06-27) the whole document	1,2, 8-16, 20-25, 31,32
X	JOUAULT T ET AL: "Peptides that mimic Candida albicans-derived beta-1,2-linked mannosides." GLYCOBIOLOGY. ENGLAND AUG 2001, vol. 11, no. 8, August 2001 (2001-08), pages 693-701, XP009026488 ISSN: 0959-6658	1-6,11, 20-24, 26-29, 31,32
Y	the whole document	1-32
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>GEIJTENBEEK TEUNIS B H ET AL: "Identification of DC-SIGN, a novel dendritic cell-specific ICAM-3 receptor that supports primary immune responses" CELL, CELL PRESS, CAMBRIDGE, NA, US, vol. 100, no. 5, 3 March 2000 (2000-03-03), pages 575-585, XP000929197 ISSN: 0092-8674 the whole document</p>	1-32
A	<p>FIGDOR CARL G ET AL: "C-type lectin receptors on dendritic cells and Langerhans cells." NATURE REVIEWS IMMUNOLOGY, vol. 2, no. 2, February 2002 (2002-02), pages 77-84, XP009026412 ISSN: 1474-1733 (ISSN print) the whole document</p>	1-32
A	<p>D'OSTIANI C F ET AL: "Dendritic cells discriminate between yeasts and hyphae of the fungus Candida albicans: Implications for initiation of T helper cell immunity in vitro and in vivo" JOURNAL OF EXPERIMENTAL MEDICINE, TOKYO, JP, vol. 191, no. 10, 15 May 2000 (2000-05-15), pages 1661-1673, XP002236580 ISSN: 0022-1007 the whole document</p>	1-32
P,Y	<p>TAYLOR PHILIP R ET AL: "The role of SIGNR1 and the beta-glucan receptor (Dectin-1) in the nonopsonic recognition of yeast by specific macrophages." JOURNAL OF IMMUNOLOGY (BALTIMORE, MD.: 1950) UNITED STATES 15 JAN 2004, vol. 172, no. 2, 15 January 2004 (2004-01-15), pages 1157-1162, XP001179812 ISSN: 0022-1767 the whole document</p>	1-32
A	<p>NEWMAN SIMON L ET AL: "Candida albicans is phagocytosed, killed, and processed for antigen presentation by human dendritic cells" INFECTION AND IMMUNITY, vol. 69, no. 11, November 2001 (2001-11), pages 6813-6822, XP002271107 ISSN: 0019-9567 the whole document</p>	1-32

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BOZZA SILVIA ET AL: "Dendritic cells transport conidia and hyphae of Aspergillus fumigatus from the airways to the draining lymph nodes and initiate disparate Th responses to the fungus." JOURNAL OF IMMUNOLOGY (BALTIMORE, MD.: 1950) UNITED STATES 1 FEB 2002, vol. 168, no. 3, 1 February 2002 (2002-02-01), pages 1362-1371, XP001179719 ISSN: 0022-1767 the whole document	1-32
P,X	WO 03 00024 A (PROGENICS PHARM INC) 3 January 2003 (2003-01-03) page 8, line 7 - line 18 page 9, line 1 -page 11, line 1 page 19, line 12 -page 20, line 8 page 52, line 23 - line 33 claims 1-154	1,2,8,9, 11-14, 16-21,31
E	WO 2004 000352 A (COLMENARES BRUNET MARIA ;CORBI LOPEZ ANGEL (ES); CONSEJO SUPERIOR) 31 December 2003 (2003-12-31) the whole document	1-32

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-8, 11, 12, 16, 20-21, 23-31 relate to compounds defined by reference to a desirable characteristic or property, namely: "a compound in an amount effective to inhibit the binding to DC-SIGN of a microorganism that binds to DC-SIGN" and / or "an antigen found in a microorganism that binds DC-SIGN".

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product/compound/method/apparatus by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds mentioned in claims 9-10, 13-15, 17-19, 22 and 32, as well as those compounds explicitly mentioned on p 9 last line - p 10 first paragraph.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

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